KMT2D gene

lysine methyltransferase 2D

Normal Function

The *KMT2D* gene, also known as *MLL2*, provides instructions for making an enzyme called lysine-specific methyltransferase 2D that is found in many organs and tissues of the body. Lysine-specific methyltransferase 2D functions as a histone methyltransferase. Histone methyltransferases are enzymes that modify proteins called histones. Histones are structural proteins that attach (bind) to DNA and give chromosomes their shape. By adding a molecule called a methyl group to histones (a process called methylation), histone methyltransferases control (regulate) the activity of certain genes. Lysine-specific methyltransferase 2D appears to activate certain genes that are important for development.

Lysine-specific methyltransferase 2D is also believed to act as a tumor suppressor, which means it normally helps prevent cells from growing and dividing in an uncontrolled way.

Health Conditions Related to Genetic Changes

Kabuki syndrome

Hundreds of mutations in the *KMT2D* gene have been identified in people with Kabuki syndrome, a disorder characterized by distinctive facial features, intellectual disability, and abnormalities affecting other parts of the body.

The *KMT2D* gene mutations associated with Kabuki syndrome change one building block (amino acid) in the lysine-specific methyltransferase 2D enzyme, delete genetic material in the *KMT2D* gene sequence, or result in a premature stop signal that leads to an abnormally short enzyme. As a result of these mutations, the enzyme is nonfunctional. A lack of functional lysine-specific methyltransferase 2D enzyme disrupts its role in histone methylation and impairs proper activation of certain genes in many of the body's organs and tissues, resulting in the abnormalities of development and function characteristic of Kabuki syndrome.

Although lysine-specific methyltransferase 2D is believed to be a tumor suppressor, a loss of this enzyme's function does not seem to increase cancer risk in people with Kabuki syndrome.

cancers

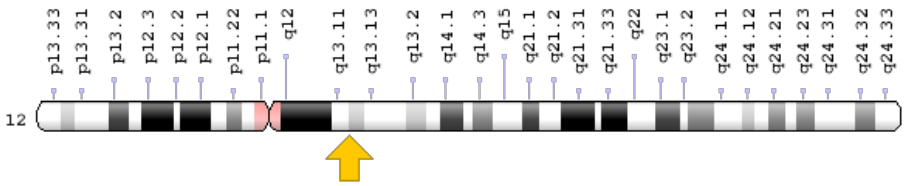
Some gene mutations occur during a person's lifetime. Such mutations, which are called somatic mutations, are present only in certain cells. Somatic mutations in the *KMT2D* gene have been identified in certain cancers. These include medulloblastomas, which are cancerous brain tumors that occur in childhood, and blood-related cancers called lymphomas. Most of these mutations result in an abnormally short, nonfunctional lysine-specific methyltransferase 2D enzyme that cannot perform its role as a tumor suppressor, resulting in the development of cancer.

Increased amounts of lysine-specific methyltransferase 2D and altered distribution of the enzyme within cells have been identified in cancerous tumors of the breast and colon. It is unknown whether these changes result primarily from increased activity (overexpression) of the *KMT2D* gene, extra copies of the gene in tumor cells, altered stability or processing of the enzyme, or other mechanisms. Excess amounts of lysine-specific methyltransferase 2D may disrupt the regulation of other genes. As a result, cells may grow and divide too quickly or in an uncontrolled way, leading to cancer.

Chromosomal Location

Cytogenetic Location: 12q13.12, which is the long (q) arm of chromosome 12 at position 13.12

Molecular Location: base pairs 49,018,975 to 49,060,884 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AAD10
- ALL1-related protein
- ALR
- CAGL114

- histone-lysine N-methyltransferase MLL2
- KMT2B
- lysine (K)-specific methyltransferase 2D
- lysine N-methyltransferase 2B
- MLL2
- MLL2_HUMAN
- MLL4
- myeloid/lymphoid or mixed-lineage leukemia 2
- TNRC21
- trinucleotide repeat containing 21

Additional Information & Resources

Educational Resources

- National Center for Biotechnology Information: Histone Modification
  https://www.ncbi.nlm.nih.gov/books/NBK45788/#epi_sci_bkgrd.Histone_modification_write

GeneReviews

- Kabuki Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK62111

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28MLL2%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- LYSINE-SPECIFIC METHYLTRANSFERASE 2D
  http://omim.org/entry/602113

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_KMT2D.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=KMT2D%5Bgene%5D

- HGNC Gene Family: Lysine methyltransferases
  http://www.genenames.org/cgi-bin/genefamilies/set/487
- HGNC Gene Family: PHD finger proteins
  http://www.genenames.org/cgi-bin/genefamilies/set/88
- HGNC Gene Family: SET domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1399
- HGNC Gene Family: Trinucleotide repeat containing
  http://www.genenames.org/cgi-bin/genefamilies/set/775
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7133
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  https://www.ncbi.nlm.nih.gov/gene/8085
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